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TITLE: Epidermal Growth Factor (EGF) Receptor Intron 1 CA Repeat Polymorphisms in African-American and Caucasian Males: Influence on Prostate Cancer Risk or Disease Progression and Interaction with Androgen Receptor CAG Repeat Polymorphisms

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13. ABSTRACT (Maximum 200 Words)

We are investigating the effect of a polymorphic epidermal growth factor receptor (EGFR) gene intron 1 CA repeat on prostate cancer (CaP) development, alone or in combination with a known androgen receptor gene CAG repeat polymorphism. We will characterize these repeats in DNA from African-American and Caucasian men with CaP. The data will be analyzed for any correlation using both parameters with clinical outcome (age of onset, rapid progression, or metastasis). The Human Subjects Protocol was approved by the US Army Medical Research and Materiel Command Human Subjects Research Review Board (USAMRMC HSRRB) on 24 November of 2003. However, the resignation of the individual who was to recruit subjects at the Cooper Hospital/ University Medical Center this year and the failure of my clinical collaborator to train a new coordinator in a timely manner has resulted in additional delays in initiating subject recruitment. Fortunately, new clinical collaborators affiliated with a major research institution have agreed to participate in the study. Since no subjects have entered the study, there is no data to report. A new Human Subjects Protocol has been submitted to the IRB and DOD HSRRB to indicate the new clinical personnel, and we anticipate initiating subject recruitment shortly.

14. SUBJECT TERMS
Genetics and molecular biology, gene interactions/transcription, familial and hereditary carcinogenesis, polymorphism/research resources

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INTRODUCTION: African-Americans are at increased risk of developing prostate cancer (CaP) relative to whites, and the lengths of two polymorphic repeats in the first exon of the androgen receptor (AR) gene contribute to that risk (Ries *et al*, 1990; Parker *et al*, 1996). The CAG repeat length is best correlated with prostate cancer risk, shorter repeats being associated with higher risk, and the prevalence of the shorter CAG alleles is greatest in African-American men, intermediate in Caucasian, and least in Asian-American men (Faber *et al*, 1989; Irvine *et al*, 1995; Kantoff *et al*, 1998; Pettaway, 1999). However, a multigenic etiology for CaP is likely. A polymorphic CA repeat has been described in intron 1 of the epidermal growth factor receptor (EGFR) gene, and the length of the repeat inversely correlated with transcriptional activity *in vitro* (Chi *et al*, 1992; Gebhardt *et al*, 1999). Preliminary evidence suggests that the CA repeat status affects EGFR content in breast cancer, and that shorter repeats might be a predisposing factor for breast cancer (Buerger *et al*, 2000). The EGFR is also important in regulation of prostatic epithelial and CaP cell growth, and androgen may affect that by increasing the levels of EGFR and its' ligands in CaP cells (Schuurmans *et al*, 1991; Liu *et al*, 1993). Shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, and potentially also by affecting alternative splicing of the EGFR transcript, could synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and promote the development of androgen-independent, metastatic prostate cancer. In collaboration with The Prostate Cancer Risk Assessment Program at Cooper Hospital/ University Medical Center, we will isolate DNA from blood samples from 300 African-American and Caucasian American men with (and some without) prostate cancer. We will determine the length of these two repeats, to determine whether the EGFR CA repeat, alone or in combination with the AR CAG repeat, affects CaP risk. Lymphoblastoid cell lines will be established for a representative subset of these samples, and will be made available to other researchers at the end of this study. The data will be analyzed for any correlation using both parameters with clinical outcome (age of onset, rapid progression, or metastasis).

BODY: Based on USAMRMC recommendation, a biostatistician, Dr. Constantine Daskalakis, was recruited to the study and a statistical analysis plan was developed. Note that the Cooper Hospital/ University Medical Center IRB considers the present study (funded by award number DAMD17-01-1-0080) to be a sub-study of the Regional Prostate Cancer Registry and Risk Assessment Program at Cooper Hospital/ University Medical Center. Previous delays in granting of approval to commence research were caused by turnover of HSRRB reviewers working with the DOD (six different reviewers) and the implementation of the new HIPAA regulations by the Cooper Hospital/ University Medical Center Institutional Review. Approval to initiate my research was finally received from the US Army Medical Research and Materiel Command Human Subjects Research Review Board (USAMRMC HSRRB) in a letter dated 24 November 2003 (Modification No. P00001 to DAMD17-01-1-0080). Taking the long delay in obtaining HSRRB approval into account, the grant performance period was extended to 30 September 2005.

Unfortunately, shortly after receiving approval to initiate subject recruitment, the individual in Dr. Marmar's office who was to carry out the recruitment and specimen collection, Juliette May, resigned her position. This occurred in January of 2004. Being assured by Dr. Marmar that a new person would be hired soon, I acquired control cell lines and initiated laboratory work with these lines (see below). Evette Ortolaza was hired as Dr. Marmar's office manager, and was to begin subject recruitment for my project (CHS RP#02-046) upon completion of training in research with

human subjects. Since she is not trained in phlebotomy, Dr. Marmar informed me that Ms. Ortolaza would not do the blood draws; rather they would be done by personnel at the Cooper Clinical Laboratory adjacent to the Urology Clinic. However, several months passed without any indication that Ms. Ortolaza had received approval from the Cooper Health System IRB for participation in research involving human subjects, despite regular communications from me. These repeated delays by my clinical collaborator in the Cooper Healthy System have prevented enrollment of any study subjects, and if continued, could pose a problem for the successful completion of this research project. Therefore, this summer I began to explore other avenues for subject enrollment, although I have kept the IRB protocol for the study at Cooper active, inasmuch as 100 samples collected under a prior protocol are available through Cooper's Regional Prostate Cancer Registry.

After investigating several avenues to recruit subjects, I am pleased to report that Drs. Raffaele Baffa and Leonard Gomella of the Department of Urology at Thomas Jefferson University in Philadelphia have agreed to participate in this research project. The Kimmel Cancer Center at Thomas Jefferson University is an NCI-Designated Cancer Center serving the greater Philadelphia area. Dr. Raffaele Baffa is Director of Urology Research, Department of Urology, and Co-Director of the Genito-Urinary Cancer Program at the Kimmel Cancer Center, and he thus works closely with Dr. Gomella. Dr. Baffa is a colleague I have known since 1993 when I was also at the Kimmel Cancer Center, and his interest in cancer genetics is longstanding (see appended curriculum vitae). Raffaele was instrumental in bringing Dr. Gomella on-board for the current research.

Dr. Gomella is Bernard W. Godwin, Jr., Professor of Prostate Cancer, Jefferson Medical College, Chairman of the Department of Urology, and Director of Urologic Oncology in the Kimmel Cancer Institute at Thomas Jefferson University. Dr. Gomella is expert in urologic oncology, with a long-standing interest in prostate cancer, as shown in his appended curriculum vitae. In addition to seeing patients and clinical work in support of basic research, he is principal investigator in a number of clinical trials. Of particular importance in the current context are his role in a longitudinal study to determine the utility of prostate-specific antigen (PSA) for early detection of prostate cancer, and in the placebo-controlled Selenium and Vitamin E Cancer Prevention Trial (SELECT A). He has been PI in these studies since 1989 and 2001, respectively. He is also principle investigator in two prostate cancer treatment trials initiated in 2003. Thus, his office has a large pool of individuals already enrolled in clinical CaP studies, both with and without cancer. Importantly, this pool includes individuals with both metastatic and non-metastatic CaP diagnosed several years ago as well as recently. Since the focus of my study is on the role of specific inherited genetic polymorphisms in CaP, prior treatment of subjects will not interfere with the results. In combination with the regular patient pool, it is anticipated that this large pool of individuals who have already demonstrated a willingness to participate in research studies will facilitate the rapid accrual of subjects for the current study, since their opportunity cost for this study is minimal.

The clinical research coordinator in the Department of Urology, Ms. Christine Hubert, will enroll subjects. Ms. Hubert has acquired extensive experience as a clinical research coordinator in a variety of studies since 1997. Christine has been at Thomas Jefferson University since 1999, exclusively as Clinical study coordinator. This experience is outlined in her appended curriculum vitae, and Ms. Hubert has already proven her reliability by quickly arranging all the materials needed for approval of the study by the Jefferson Clinical Cancer Research Review Board (CCRRC).

Since no new subjects have been enrolled, there is no data to report. The Human subjects documents and new curriculum vitae are appended.

KEY RESEARCH ACCOMPLISHMENTS: New clinical collaborators at an NCI-designated Cancer Center have agreed to participate in subject recruitment (Task 1a). This is key to enrolling sufficient subjects for successful completion of the study. Control cell lines have been acquired and grown, and DNA has been isolated from these lines. My technician has been trained in isolation of mononuclear cells from blood, and in DNA isolation (these activities are part of Task 2b). PCR analyses of control cell lines are underway. No other results are yet available, since we have not been able to recruit any subjects to date.

REPORTABLE OUTCOMES: None.

CONCLUSIONS: Despite tremendous progress in research into the origins of prostate cancer (CaP), there are still many important, unresolved questions about the etiology of this common cancer. Perhaps the most urgent problem facing prostate cancer researchers -- and those with the disease -- is to identify the subset of CaP sufferers whose cancer will progress rapidly. Despite extensive research, no single marker has arisen as a definitive marker of such cancers. Indeed, a multigenic etiology for CaP is extremely likely. Among the candidate genes are those encoding the androgen receptor and the epidermal growth factor receptor (EGFR). The EGFR is clearly important in the regulation of prostatic epithelial and CaP cell growth, and is frequently overexpressed in BPH and CaP cells, but no studies have convincingly demonstrated that it is of great use in predicting the course of a particular CaP case. However, a polymorphic CA repeat has been described in intron 1 of the epidermal growth factor receptor (EGFR) gene, and the length of the repeat has recently been inversely correlated with transcriptional activity *in vitro* (Chi *et al*, 1992; Gebhardt *et al*, 1999). Androgen may also influence the expression of the EGFR by increasing the levels of its' ligands, and perhaps directly in CaP cells (Schuurmans *et al*, 1991; Liu *et al*, 1993). However, the possible contribution of EGFR CA repeat polymorphisms on prostate cancer risk or progression has never been investigated. Shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, and potentially also by affecting alternative splicing of the EGFR transcript, could synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and promote the development of androgen-independent, metastatic prostate cancer. No work addressing these issues with respect to CaP has been published to date, although Buerger *et al* recently reported (2004) new results associating the allelic length of the EGFR CA repeat with EGFR gene amplification in breast cancers. This proposal will address these possibilities, and will also provide resources for definitive future studies.

Given that only the site for subject recruitment and personnel have changed (and improved), we anticipate ready approval of the revised human subjects research protocol and expeditious recruitment of the research subjects.

It is important to emphasize that subject recruitment is the limiting factor in this research. The mononuclear cell isolation, DNA extraction, and polymerase chain reaction (PCR) analyses are standard techniques with which the investigators have extensive experience, and large numbers of samples can be analyzed in a short period of time.

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HSRRB Log No. A-10414/ PC001407 - " Epidermal Growth Factor (EGF) Receptor intron 1 CA repeat polymorphisms in African-American and Caucasian males: Influence on Prostate Cancer risk or disease progression and interaction with Androgen receptor CAG repeat polymorphisms."

Human Subjects Protocol

1. This grant will utilize specimens and information accrued through The Prostate Cancer Risk Assessment Program, a collaborative project of Cooper Hospital/ University Medical Center and The Coriell Institute for Medical Research. The overall study is entitled "Development of a regional prostate cancer registry & risk assessment program".

2. This protocol does NOT involve the testing of Investigational New Drugs or Devices.

3. Principal Investigator (PC001407):

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5. Time required to complete: Expected Start: 24 November, 2003
Completion: 31 September, 2005

6 - 9. Protocol

a. Research Hypotheses/ Objectives: This study involves the development of a prostate cancer database that will collect data not currently available on prostate cancer patients and their family members. Personal information and blood samples will be collected from all participants, and tissue samples will be collected from participants that undergo medically indicated biopsies or surgeries. Regarding PC001407, I hypothesize that shorter CA repeats in intron 1 of the EGFR gene, by resulting in transcriptional enhancement of EGF receptor expression, will synergize with shorter CAG androgen receptor AR repeats to increase the risk of early onset prostate cancer and/ or promote the development of androgen-independent, aggressive prostate cancer. The status of Epidermal Growth Factor (EGF) Receptor intron 1 CA repeat and androgen receptor CAG repeat polymorphisms in African-American and Caucasian males will be determined by PCR analysis of DNA isolated from blood samples. These data will be studied in conjunction with the personal and medical information to determine whether the status of the EGF receptor polymorphism, alone or in combination with the androgen receptor polymorphism, influences the age of ons et or biological characteristics (e.g., hormone dependence, invasiveness, metastasis) of prostate cancer. Further details are described in the included abstract.

b. Study Population: The study population will be comprised of approximately 300 males recruited from individuals who come to the Department of Urology at Thomas Jefferson University for prostate cancer treatment or screening, and to Cooper Hospital for the treatment of prostate cancer and via the Prostate Cancer Risk Assessment Program at Cooper Hospital. Cooper Hospital serves primarily Camden County and western Burlington County, New Jersey, and ethnically diverse area with significant African-American, Caucasian, and Hispanic populations.

c. Inclusion and Exclusion Criteria: All subjects recruited will be males in the age range of 35 - 69 years. Carcinoma of the prostate (CaP) is rare among individuals under age 35, whereas prostatic intraepithelial neoplasia (PIN) the presumed precursor of CaP, is very common among men older than 70, so older individuals are less likely to be informative regarding hereditary predisposition. Because the frequency of the various EGF receptor intron 1 CA repeat lengths in African-American men is currently unknown, and since African-American men are at greater risk of prostate cancer than the general population, we will recruit a significant fraction of subjects from the African-American community. Subjects accrued to date under the previously approved Prostate Cancer Risk Assessment Program protocol are ca. 50% African-American and 50% Caucasian.

d. Informed Consent Process: The Clinical Study Coordinator in the Department of Urology at Thomas Jefferson University or Clinical nursing staff at Cooper Hospital/University Medical Center will explain The Prostate Cancer Risk Assessment Program in lay terms to prospective subjects who come to the weekly screening clinic ("self-recruitment"). The Prostate Cancer Risk Assessment Program is open to men between the ages of 35 and 69 who are African-American, or of any race with a family history of prostate cancer. Prostate cancer patients of Dr. Joel Marmar will also be offered the opportunity to enroll in the study. Individuals uncertain about participation may discuss the study with friends and family members and return at a later time. Interested individuals will then be talked through the informed consent form (appended), with particular attention being focussed on the clauses regarding (a) the choice to be informed of any clinical implications of their results in the context of this or other relevant prostate cancer studies, (b) the risks of participation in the study, and (c) sample donation. Witnesses may be other clinic personnel or any other individual the subjects choose. As the document is discussed, the subjects and their witnesses will be asked to initial each page to indicate that it has been explained to them, as well as to sign the last page of the document to indicate their agreement to participate in the study. Two copies of the consent form will be completed so that the subjects can keep an original copy.

e. Sample Size: A target of 300 individuals will be sought over the course of 3 years. (The overall target for the Regional Prostate Cancer Registry and Risk Assessment Program is 400 subjects, but the time and funds for PC001407 will allow for analysis of 300.) By recommendation of peer review, a biostatician has been consulted regarding sample size (appended), and will be consulted for subsequent data analyses. EGFR intron 1 CA repeat allele frequencies in the general populations of African-American and Caucasian American men will be determined by analysis of DNA samples from apparently normal individuals in existing Coriell Cell Repository panels.

f. Protocol Design: Male subjects (300) will be recruited from individuals who come for screening or treatment of prostate cancer and via the Prostate Cancer Risk Assessment Program at Cooper Hospital as described in b - d above. Notices will be published as in the appended Cooper Health system newsletter. After informed consent is obtained as described in (d), subjects will be asked to complete a Health History Questionnaire (appended), and to donate 3 (~10 ml each) tubes of blood. One tube will be used by the hospital for medical diagnosis (e.g., Prostate Specific Antigen

level), while the other tubes will be used at the Coriell Institute for Medical Research for (a) extraction of DNA and (b) isolation and cryopreservation of lymphocytes. Blood will be collected no more than once per year for the purposes of this study. The lengths of the EGFR intron 1 CA repeat and the AR CAG repeat will be determined by PCR analysis of the DNA (of the samples accrued to date on a previous protocol, the AR repeat has already been analyzed in several dozen). Epstein-Barr virus-immortalized lymphoblastoid cell lines will be established for individuals representing the possible combinations of these two polymorphisms. These cell lines will be deposited in the National Institute of Aging Repository in the Coriell Cell Repositories, and will be available to other researchers at the end of this study. We will also utilize prostate biopsies, when obtained as part of the subjects' medical care, to examine EGFR and AR expression and initiate prostate cell lines. The specimens, health histories, and clinical information will be encoded as PS### (e.g., PS100, PS101, etc.) by the Cooper Hospital clinical staff, such that all specimens and information received by The Coriell Institute for Medical Research will be separated from subject names. Coriell will receive only coded summaries of the Health History Questionnaires. Any cell lines accepted by the Coriell Cell Repositories for distribution to other researchers will be given new code numbers (e.g., AG00000) to ensure confidentiality. For PS### cell lines to be submitted to the Coriell Cell Repositories, Dr. Joel Marmar's clinical staff will assign new numbers from a list of the next available AG numbers; the list indicating the PS #s corresponding to the new AG numbers will be kept by his office for 4 years after completion of the study.

g. Risks to Subjects: As this is not an interventional protocol, this project poses no greater than minimal risk to participants. Risks noted in the consent form include the risk of discovering a genetic predisposition to cancer, which may cause concern. Subjects may also have concerns even if they are not in the future told that they have a gene alteration that has been linked to an increased risk of prostate cancer. Subjects do not have to agree to have this information revealed to them or their family members. The risks and discomfort associated with giving blood include the possibility of bleeding and bruising. This rarely causes a significant problem.

h. Benefits to Subjects: As noted in the consent form, subjects will not receive any immediate benefits as a result of participation in this study. It is possible that the study will reveal known or novel genetic polymorphisms that would indicate a statistically greater or lesser prostate cancer risk than the general population. This might prompt an individual to have regular screening for prostate cancer, which could affect their prognosis should cancer be discovered. However, such information is more likely to be of use in the future, rather than to subjects recruited in the current study.

i. Roles and Responsibilities of Study Personnel: Local review boards have not found the protocol to be of greater than minimal risk, so no medical monitor has been assigned.

David K. Moscatello, Ph.D. Role: Principal Investigator (PC001407), 40%. Lymphocyte and DNA isolation, analysis of EGFR intron 1 CA repeats, analysis of Androgen receptor CAG repeats, preparation of DNA, RNA, and protein lysates from prostate specimens, immunohistochemistry and western blotting, reverse transcription-polymerase chain reaction (RT-PCR), Southern and Northern blotting, cryopreservation of viable prostate biopsies, and data analysis.

Bender, Patrick K., Ph.D. (Associate Professor and Supervisor, Division of Molecular Biology, Coriell Institute for Medical Research, 5%. Role: Analysis of Androgen Receptor CAG repeats.

Leonard Gomella, M.D., (Professor of Urology , Director, Urologic Oncology & Chairman, Dept. of Urology, Kimmel Cancer Center, Thomas Jefferson University. Role: subject recruitment.

Raffaele Baffa, M.D. (Associate Professor, Director of Urology Research and Co-Director Genito-Urinary Cancer Program, Department of Urology, Kimmel Cancer Center, Thomas Jefferson University). Role: subject recruitment.

Christine Hubert, B.A. (Clinical Study Coordinator, Department of Urology, Thomas Jefferson University). Role: subject recruitment, interviews, data entry and encoding.

Grana, Generosa, M.D., Assistant Professor of Hematology/ Oncology and Medical Director, The Cancer Risk Evaluation Center, Cooper Hospital/University Medical Center, 5%. Role: Medical Director, The Cancer Risk Evaluation Center.

Marmar, Joel, M.D., Professor of Urology and Head, Division of Urology, Cooper Hospital/ University Medical Center, 5%. Role: Procurement of benign and malignant prostate specimens.

Milagro Concepcion, B.A., Technician, Coriell Institute for Medical Research, 50%. Role: Lymphocyte isolation and cryopreservation, DNA isolation, and PCR.

Constantine Daskalakis, Sc.D., Biostatistics section of the Department of Medicine, Thomas Jefferson University, Philadelphia, PA, 5%. Role: Consultant for study design and data analyses.

10. Reporting of serious and unexpected adverse events. This is not an IND or IDE protocol. No medical interventions are proposed. However, there is a remote possibility of a severe adverse event such as excessive bleeding or infection as a result of blood collection. Should such an event occur, Adverse experiences that are both serious and unexpected will be immediately reported by telephone to the USAMRMC Deputy for Regulatory Compliance and Quality (301-619-2165) and send information by facsimile to 301-619-7803). A written report will follow the initial telephone call within 3 working days.

11. Description of Protocol Drug(s) or Device(s): Not applicable.

12. Disposition of data: All health history and clinical records will be maintained at Thomas Jefferson University Hospital or Cooper Hospital/ University Medical Center according to their standard procedures. No disposal is contemplated, except for individuals who are withdrawn from the study (either voluntarily or otherwise), in which case the health questionnaires held at Cooper, and samples and associated data held at Coriell will be destroyed. Otherwise, encoded/ tabulated data without personal identifiers of just the subset of samples that will be submitted to the NIA Cell Repository will be maintained in the secure files of The Coriell Institute for Medical Research indefinitely.

13. Modification of the protocol: As this is not an IND/ IDE protocol, no modifications are anticipated, with the possible exception of the recruitment of additional subjects. This might be necessary to achieve statistical validity of possible correlations between the genetic polymorphisms and clinical data. The use of additional methods to recruit subjects might be considered if targets are not met. If this becomes necessary, the revisions, including any proposed new recruiting methods, will be submitted to the Institutional Review Boards of both local institutions, and subsequently to the OTSG HSRRB for approval.

14. Departure from the Protocol: Any departures from the proposed protocol with respect to the consents, questionnaires, or specimens will be submitted to the Institutional Review Boards of both local institutions, and subsequently to the OTSG HSRRB.

15. Roles and Responsibilities of Study Personnel: See (i) above.

16. USAMRMC Volunteer Registry Database: Project judged not greater than minimal risk by local review boards, therefore not applicable.

Signature of Principal Investigator: _____

David K. Moscatello, Ph.D.

Date: _____

STATISTICAL ANALYSIS PLAN

Our analyses will be based on samples obtained from 300 prostate cancer patients (prospectively collected) and from approximately 200 controls (from existing panels). The study's aims are to evaluate
(1) the association between EGFR intron 1 CA repeats and prostate cancer;
(2) the association between AR CAG repeats and prostate cancer; and
(3) the combined (synergistic) effect of EGFR and AR on prostate cancer.

The first two aims pertain to the main effect of each gene, while the third aim focuses on their possible interaction. Preliminary analyses will be based on two-by-two cross-classification tables of each gene with prostate cancer status (case/control). We will estimate and test the (crude) unadjusted odds ratio separately for each gene, using Fisher's exact test and Mantel-Haenszel stratification analysis. We will then model the outcome (prostate cancer case or control status) as a function of both genes via logistic regression. In this multivariable analysis, we will also control for age, race, and other potential confounders.

Finally, we will test the hypotheses of "no multiplicative interaction" and "no additive interaction" between the two genes. Using the long-EGFR/long-AR combination as the referent group, the hypothesis of no multiplicative interaction implies that the joint odds ratio for the short-EGFR/short-AR combination is equal to the product of the two main effects odds ratio (i.e., short-EGFR/long-AR and long-EGFR/short-AR). The test of this hypothesis involves testing the product interaction term; likelihood ratio and Wald tests are straightforward to compute in all statistical packages. The hypothesis of no additive interaction, on the other hand, implies that the joint odds ratio is the sum of the two main effects odds ratios minus one. Although preprogrammed software capabilities do not allow testing of this hypothesis in logistic regression, we have a SAS macro that will allow us to perform the corresponding likelihood ratio and Wald tests.

We have also planned secondary analyses to assess:
1. the effects of the two genes among Caucasian and African-American subjects (i.e., gene-by-race interactions); and
2. the association between the length of the repeats for each gene and cancer recurrence and/or survival (among the prostate cancer cases only).

SAMPLE SIZE AND POWER

Based on previous data, EGFR intron 1 CA repeats show a distribution with 3 peaks in the general population, at 20, 18 and 16 repeats. A smaller number of repeats (<17, approximately 45% in the general population) are hypothesized to be associated with higher risk of prostate cancer. With 300 cases and 200 controls, using a two-tailed Fisher's exact test with alpha of 0.05, we have 84% power to detect an odds ratio of about 1.75 (i.e., short allele in 45% of the controls vs. 59% of the cases).

Similarly, based on previous data, AR CAG short repeats (<20) seem to be present in about 30% of the general population. With 300 cases and 200 controls, using a two-tailed Fisher's exact test with alpha of 0.05, we have 82% power to detect an odds ratio of 1.75 (i.e., short allele in 30% of the controls vs. 43% of the cases).

In terms of the interaction between the two genes, we have good power to detect moderate interactions on both the additive and the multiplicative scale. All power calculations were performed via Monte-Carlo simulation, using the appropriate likelihood ratio tests in logistic regression, with alpha of 0.05.

Assuming main effect odds ratios for each gene of about 1.75, under the "no additive interaction hypothesis", we expect a joint odds ratio of 2.5 (i.e., 1.75+1.75-1) for the comparison of the short-EGFR/short-AR combination with the referent long-EGFR/long-AR combination. In our study, we have power to detect departures from additivity when the synergy factor is 3 or higher (i.e., an odds ratio for the joint effect of 5.5 or higher):

Allele EGFR	Allele AR	Effect type	OR	OR	Power	OR	Power
long	long	refer.	1.00				
long	short	main	1.75				
short	long	main	1.75				
short	short	joint	2.50*	5.5	81%	6.5	91%

(*) Additivity of effect (i.e., no additive interaction)

With the same assumptions of main effect odds ratios for each gene of about 1.75, under the "no multiplicative interaction hypothesis", we expect an odds ratio of 3.06 (i.e., 1.75x1.75) for the comparison of the short-EGFR/short-AR combination with the referent long-EGFR/long-AR combination. In our study, we have power to detect a multiplicative interaction factor of about 3 or higher (i.e., an odds ratio for the joint effect of 9 or higher):

Allele EGFR	Allele AR	Effect type	OR	OR	Power	OR	Power
long	long	refer.	1.00				
long	short	main	1.75				
short	long	main	1.75				
short	short	joint	3.06*	9.2	75%	10.7	85%

(*) Multiplicativity of effect (i.e., no multiplicative interaction)

Constantine Daskalakis, ScD
Assistant Professor,
Biostatistics Section, Thomas Jefferson University,
125 S. 9th St. #402, Philadelphia, PA 19107
Tel: 215-955-5695
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Email: constantine.daskalakis@mail.tju.edu

Principal Investigator/Program Director (Last, First, Middle): Moscatello, David K, Ph.D.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Moscatello, David Keith	Assistant Professor, Coriell Institute for Medical Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Pennsylvania State University, University Park,	B.S.	1971-1975	Microbiology
Purdue University, West Lafayette, IN	Ph.D.	1975-1984	Biology
Thomas Jefferson University, Philadelphia, PA	Post-Doc	1992-1997	Molecular Biology

A. Positions and Honors

Positions and Employment

1984-1987 Visiting Instructor of Microbiology, Dept. of Biological Sciences, Purdue University, West Lafayette, Indiana

1987-1992 Assistant Professor of Biology, Division of Natural and Mathematical Sciences, Richard Stockton College of New Jersey, Pomona, New Jersey

1992-1997 Postdoctoral Research Fellow in the laboratory of Albert J. Wong, M.D., Department of Microbiology and Immunology, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA

1997-1999 Research Instructor, Department of Microbiology and Immunology, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA

1999-Present Assistant Professor and Supervisor, Differentiated Cell Laboratory, Coriell Institute for Medical Research, Camden, NJ

Other Experience And Professional Memberships:

1981-1984 Graduate Instructor of Microbiology, Dept. of Biological Sciences, Purdue University

1987-present Member, American Association for the Advancement of Science

1990-1997 Board member, Atlantic County Unit, American Cancer Society

1991-1993 Consultant for the Public Health Technical Resource Center (Richard Stockton College of New Jersey, Pomona, NJ).

1998-present Member, American Association for Cancer Research

2001-present Member, American Association for Cell Biology

2003-2004 Member, Coriell Institute for Medical Research Board of Trustees

Honors:

1980-1981 David Ross Graduate Fellowship

1990 Stockton State College Distinguished Faculty Fellowship

1995-1997 National Institutes of Health Postdoctoral Research Fellowship

B. Selected peer-reviewed publications (in chronological order).

1. Moscatello, D.K., Holgado-Madruga, M., Godwin, A.K., Ramirez, G., Gunn, G., Zoltick, P.W., Biegel, J.A., Hayes, R.L., and Wong, A.J. Frequent expression of a mutant Epidermal Growth Factor receptor in multiple human tumors. Cancer Res. 55, 5536-5539, 1995.
2. Montgomery, R.B., Moscatello, D.K., Wong, A.J., Cooper, J.A., and Stahl, W.L. Differential modulation of MEK and MAP kinase activities by a mutant EGF receptor. J. Biol. Chem. 270, 30562-30566, 1995.
3. Holgado-Madruga, M., Emlet, D.R., Moscatello, D.K., Godwin, A.K., and Wong, A.J. A Grb2-associated docking protein in EGF- and insulin-receptor signaling. Nature 379, 560-564, 1996.
4. Moscatello, D.K., Montgomery, R.B., Sundareshan, P., McDanel, H., Wong, M.Y., and Wong, A.J. Transformation and altered signal transduction by a naturally occurring mutant EGF receptor. Oncogene 13, 85-96, 1996.
5. Moscatello, D.K., Ramirez, G., and Wong, A.J. A naturally occurring mutant human epidermal growth factor receptor as a target for peptide vaccine immunotherapy of tumors. Cancer Res. 57, 1419-1424, 1997.
6. Holgado-Madruga, M., Moscatello, D.K., Emlet, D.R., Dieterich, R., and Wong, A.J. Gab1 mediates phosphatidylinositol 3-kinase activation and the promotion of cell survival by nerve growth factor. Proc. Natl. Acad. Sci. USA, 94, 12419-12424, 1997.
7. Montgomery, R.B., Moscatello, D.K., Wong, A.J., and Stahl, W.L. Epidermal growth factor receptor stimulation of diacylglycerol kinase. Biochem. Biophys. Res. Comm. 232, 111-116, 1997.
8. Emlet, D.R., Moscatello, D.K., Ludlow, L.B., and Wong, A.J. Subsets of epidermal growth factor receptors during activation and endocytosis. J. Biol. Chem. 272, 4079-4086, 1997.
9. Moscatello, D.K., Holgado-Madruga, M., Emlet, D.R., Montgomery, R.B., and Wong, A.J. Constitutive activation of phosphatidylinositol 3-kinase by a naturally occurring mutant epidermal growth factor receptor. J. Biol. Chem. 273, 200-206, 1998.
10. Moscatello, D.K., Santra, M., Mann, D.M., McQuillan, D.J., Wong, A.J., and Iozzo, R.V. Decorin suppresses tumor cell growth by activating the epidermal growth factor receptor. J. Clin. Invest. 101, 406-412, 1998.
11. Antonyak, M., Moscatello, D.K., and Wong, A.J. Constitutive activation of c-Jun N-terminal kinase by a mutant epidermal growth factor receptor. J. Biol. Chem. 273, 2817-2822, 1998.
12. Iozzo, R.V., Moscatello, D.K., McQuillan, D.J., and Eichstetter, I. Decorin is a biological ligand for the Epidermal Growth Factor Receptor. J. Biol. Chem. 274, 4489-4492, 1999.
13. Maroun C.R., Moscatello, D.K., Naujokas, M.A., Holgado-Madruga, M., Wong, A.J., Park, M. A conserved inositol phospholipid binding site within the pleckstrin homology domain of the Gab1 docking protein is required for epithelial morphogenesis. J. Biol. Chem. 274(44), 31719-31726, 1999.
14. Olapade-Olaopa E.O., Moscatello, D.K., MacKay, E.H., Horsburgh, T., Sandhu, D.P.S., Terry, T.R., Wong A.J., and Habib F.K. Evidence for the differential expression of a variant EGF receptor protein in human prostate cancer. British Journal of Cancer. 82(1), 186-194, 2000.
15. Tang, C.K., Gong, X-Q., Moscatello, D.K., Wong, A.J., and Lippman, M.E. EGFRvIII enhances tumorigenicity in Human Breast Cancer. Cancer Research 60, 3081-3087, 2000.

16. Olapadè-Olaopa, E.O., Ogunbiyi, J.O., MacKay, E.H., Muronda, C.A., Alonge, T.O., Danso, A.P., Moscatello, D.K., Sandhu, D.P., Shittu, O.B., Terry, T.R., Wong, A.J., and Habib, F.K. Further characterization of storage-related alterations in immunoreactivity of archival tissue sections and its implications for collaborative multicenter immunohistochemical studies. Appl. Immunohistochem. Mol. Morphol. (3): 261-266, 2001.
17. Moscatello, D.K. and Iozzo, R.V. Interaction of Proteoglycans with Receptor Tyrosine Kinases. *In* Proteoglycan Protocols, Methods in Molecular Biology 171, Renato V. Iozzo, Ed. Humana Press, Totowa, New Jersey, pp. 427-434, 2001.
18. Antonyak M.A., Kenyon L.C., Godwin A.K., James D.C., Emlet D.R., Okamoto I., Tnani M., Holgado-Madruga M., Moscatello D.K., Wong A.J. Elevated JNK activation contributes to the pathogenesis of human brain tumors. Oncogene 21(33): 5038-5046, 2002.
19. Modjtahedi H., Moscatello D.K., Box G., Green M., Shotton C., Lamb D.J., Reynolds L.J., Wong A.J., Dean C., Thomas H., Eccles S. Targeting of cells expressing wild-type EGFR and type-III mutant EGFR (EGFRvIII) by anti-EGFR MAb ICR62: A two-pronged attack for tumour therapy. Int. J. Cancer. 2003 Jun 10; 105(2): 273-80.
20. Moscatello D.K., Dougherty M., Narins R.S., and Lawrence N. Cryopreservation of human fat for soft tissue augmentation: Viability requires use of cryoprotectant and controlled freezing and storage. Derm. Surg. (in press, 2004).

C. Research Support

Ongoing Research Support

BCS-0421304 Hanner (PI) 8/1/04-7/31/07
NSF Major Research Instrumentation Program:
Acquisition and testing of the ImageStream 100 (beta model): Improving quality and expanding the scope of the Integrated Primate Biomaterial and Information Resource.
Role: Application development

DAMD17-01-1-0080 Moscatello (PI) 9/01/03-8/31/05
DOD/USAMRMC
Epidermal growth factor (EGF) receptor intron 1 repeat polymorphisms in African-American and Caucasian males: Influence on prostate cancer risk or disease progression and interaction with androgen receptor CAG repeat polymorphisms.
Role: PI

NO1-GM-9-2102 Coppock (PI) 9/17/99 - 9/16/04
NIGMS
Title: Human Genetic Cell Repository
Role: Supervisor, Differentiated Cell Laboratory (Isolation and characterization of differentiated cells)

NO1-AG-1-2101 Coppock (PI) 1/31/00-12/31/09
NIH/NIA

Selection, Production, Characterization, and Distribution of Genetically Marked Cells for Aging Research, National Institute on Aging. The Coriell Institute produces, characterizes, and distributes cell cultures worldwide for aging-related research under this contract.
Role: Supervisor Differentiated Cell Laboratory (Isolation and characterization of differentiated cells)

Completed Research Support

(No grant number) Moscatello (PI) 1/1/03 – 12/31/03
Ronald McDonald House of Southern New Jersey
Optimization of Culture Conditions for Pancreatic Islets and Expansion and Differentiation of Pancreatic Islet Stem Cells
Role: PI

(No grant number) Moscatello (PI) 1/1/03 – 12/31/03
Lawrence C. Fuller, Jr., Memorial Diabetic Fund
Equipment for Optimization of Culture Conditions for Pancreatic Islets and Expansion and Differentiation of Pancreatic Islet Stem Cells
Role: PI

(No grant number) Moscatello (PI) 11/1/01-10/31/02
American Society for Dermatologic Surgery (ASDS)
Novel Methods for the Isolation, Culture, and Cryopreservation of Human Adipocytes and Adipose Stromal Cells from Tumescent Liposuction Procedures. Methods for manipulating and preserving human adipocytes (fat cells) for clinical and research uses were established.
Role: PI

(No grant number) Moscatello (PI) 8/1/00 - 8/15/01
Lawrence C. Fuller, Jr., Memorial Diabetic Fund
Establishment of a Novel Hybrid Thymic Organ Culture System for Diabetes Research
A thymic epithelial-stromal co-culture system for studies of T-cell development *in vitro* was established.
Role: PI

D. Patent Applications:

"Sensitive Detection of Wild-Type and Mutant EGFR by Specific Elisa Assays in Any Biological Sample", Kim Leitzel, David K. Moscatello, Alan Lipton, and Albert J. Wong, co-inventors. U.S. patent application submitted March 2000.

"Reagents and Processes for Targeting Mutant Epidermal Growth Factor Receptors", Albert J. Wong and David K. Moscatello, co-inventors. U.S. and international patents pending.

Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form for the initial budget period.

NAME	POSITION TITLE
JOEL LESLIE MARMAR, M.D.	Professor of Urology and Head, Division of Urology, Department of Surgery

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
Franklin and Marshall College, Lancaster, PA	B.S.	1960	Biology
University of Pennsylvania School of Medicine Philadelphia, PA	M.D.	1964	Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

1964-65 INTERNSHIP, Rotating, Albert Einstein Medical Center, Philadelphia, PA
1965-66 RESIDENCY: General Surgery, Jeanes Hospital, Fox Chase, Pennsylvania
1966-69 RESIDENCY: Urology, Temple University Hospital, Philadelphia, PA
1969-71 Major/Medical Corps, U.S. Army, Chief of Urology, 24th Evacuation Hospital, Vietnam
1984 - Present Professor of Urology, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson School of Medicine at Camden
1993 - Present Medical Director, Fertility Testing Laboratory, Philadelphia, PA

CERTIFICATION:
Urology, 1973 - American Board of Urology
Fellow, 1974 - American College of Surgeons

OTHER TRAINING:
Urologic Microsurgery Course. September 1980 University of Louisville, Louisville, Kentucky

Urologic Laser Surgery Course, September 1983, Temple University Hospital, Philadelphia, PA

Lithotripter Training, November 4-9, 1985, EDAP Instrument, Hospital Pont de Choisyes, Paris, France
Dornier HM3, Hospital Necker, Paris, France

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

OTHER TRAINING (Cont'd.):	Additional Lithotripter Training, November 13-20, 1988 Direx Instrument, University de Liege au Bart Tilman, Liege, Belgium University Hospital, Maastrik, Holland Jeanne d'Arc Polyclinic, Lyon, France Laparoscopy Training, Worldwide Veterinary Services Parsippany, NJ March 1991 Laser Prostatectomy Training, May 1992 J.R. Bard Co., Chicago, Illinois May 1992 Prostate Cryosurgery Training, January 28 - February 1, 1994 Widdington Hospital (Graham Watson, M.D.), London, England Prostate Surgery with TUNA (transurethral needle ablation) Philadelphia, PA June 1, 1997
HONORS AND AWARDS:	Phi Beta Kappa, 1960 Student Research Award, 1964 Undergraduate Medical Society University of Pennsylvania School of Medicine Certificate of Appreciation (Vietnam Service) 1970 Armed Forces of the United States Recognition Award, 1983, Leadership in the Field of Andrology Cooper Hospital/University Medical Center
LICENSURE:	State of New Jersey - MA24609 State of Pennsylvania - MD008116E State of Florida - ME0015259
MILITARY SERVICE:	Major/Medical Corps United States Army, 1969-71 Chief of Urology, 24th Evacuation Hospital, Vietnam

Biographical Sketch

NAME	POSITION TITLE
Constantine Daskalakis	**Assistant Professor**

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Athens (Greece)	B.S.	1989	Biology
University of Massachusetts (Amherst, MA)	M.S.	1992	Epidemiology
Harvard University (Boston, MA)	Sc.D.	1997	Biostatistics & Epidemiology

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

Professional Experience:

2000 - Present Assistant Professor, Department of Medicine, Thomas Jefferson University
1997 - 2000 Research Fellow, Department of Biostatistics, Harvard University
1993 - 1996 Teaching Fellow, Department of Biostatistics, Harvard University
1992 - 1996 Research Assistant, Department of Epidemiology, Harvard University
1987 - 1991 Research Assistant, Department of Biostatistics & Epidemiology, University of Massachusetts

Honors and Awards:

1995 Teaching Assistant of the Year Award, Harvard School of Public Health
1994 Robert B. Reed Prize of Biostatistics, Department of Biostatistics, Harvard School of Public Health

Publications:

Zahner GEP, **Daskalakis, C.** Modeling sources of informant variance in parent and teacher ratings of child psychopathology. *Int J Meth Psych Res* 1998; 7: 3-16.

Zahner GEP, **Daskalakis C.** Factors associated with mental health, general health, and school-based service use for child psychopathology. *Am J Public Health* 1997; 87: 1440-1448.

Hauser R, **Daskalakis C,** Christiani DC. Regression approach to the analysis of serial peak flow among fuel oil ash exposed workers. *Am J Respir Crit Care Med* 1996; 154: 974-980

Fitzmaurice GM, Laird NM, Zahner GEP, **Daskalakis C.** Bivariate logistic regression analysis of childhood psychopathology ratings using multiple informants. *Am J Epidemiol* 1995;142: 1194-1203.

Daskalakis C, Goldberg RJ, Ockene JK, Kalan K, Hosmer DW, Pbert L. Comparison of patients' and their resident physicians' responses regarding smoking-cessation interventions. *Acad Med* 1993; 68: 168-170.

Daskalakis C, Shenassa ED. The connection between R^2 and sensitivity and specificity in the case of a dichotomous outcome. *The American Statistician* (submitted).

Daskalakis C, Murphy JM, Laird NM. Multivariate analysis of outcomes from multiple sources: A short-interval study of depression. *Am J Epidemiol* (submitted).

Daskalakis C, Lard NM, Lipsitz SR. Simultaneous modeling of mean response and association for multivariate categorical outcomes. *Biostatistics* (submitted).

Daskalakis C, Lipsitz SR. Assessing additive interactions in logistic regression. *Biometrics* (submitted)

Biographical sketch

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
GOMELLA, Leonard G., MD	**Professor**

EDUCATION *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Queens College, SUNY, New York	BA	1976	Biology
University of Kentucky, Lexington, KY	MD	1980	MD
University of Kentucky, Lexington, KY	Internship	1982	General Surgery
University of Kentucky, Lexington, KY	Residency	1986	Urology

PROFESSIONAL EXPERIENCE:

1986-1988 Fellow, Urologic Oncology, Surgery Branch, NCI, NIH Bethesda, MD
1988-1993 Assistant Professor, Department of Urology, Jefferson Medical College
1993-2002 Associate Professor, Department of Urology, Jefferson Medical College
1996-Present Director, Urologic Oncology, Kimmel Cancer Center, Thomas Jefferson University
2002-Present Chairman, Urology Department, Jefferson Medical College, Thomas Jefferson University

HONORS AND AWARDS:

1994-2002, Bernard W. Godwin Jr. Associate Professor of Prostate Cancer, Jefferson Medical College
2002-Present Bernard W. Godwin, Jr., Professor of Prostate Cancer, Jefferson Medical College

SCIENTIFIC PUBLICATIONS: (Selected from 160 Articles and Chapters)

1. Halpern, EJ, Gomella, LG, Pseudomass of the bladder neck after prostatectomy: report of two cases. Radiology, 2003, Mar; 226 (3):833-5
2. Halpern, E. J., Frauscher, F., Strup, S. E., Nazarian, L. N., O'Kane, P., and Gomella, L. G. Prostate: high frequency Doppler US imaging for cancer detection, Radiology. 2002, Oct: 25(1): 71-7
3. Halpern, E. J., Frauscher, F., Rosenberg, M., and Gomella, L. G. Directed biopsy during contrast-enhanced sonography of the prostate, AJR Am J Roentgenol.2002 Apr 178 (4): 915-9.,
4. Halpern, E. J., Frauscher, F., Forsberg, F., Strup, S. E., Nazarian, L.N., O'Kane, P., and Gomella, L. G. High-frequency Doppler US of the prostate: effect of patient position, Radiology. 2002. Mar, 222: 634-9.
5. Halpern, E. J., McCue, P. A., Aksnes, A. K., Hagen, E. K., Frauscher, F., and Gomella, L. G. Contrast-enhanced US of the prostate with Sonazoid: comparison with whole-mount prostatectomy specimens in 12 patients, Radiology. 2002, 222 (2): 361-6.
6. Lee, D., Trabulsi, E., McGinnis, D., Strup, S., Gomella, L. G., and Bagley, D. Totally endoscopic management of upper tract transitional-cell carcinoma, J Endourol. 2002, Feb;16 (1): 37-41.
7. Vecchione, A., Ishii, H., Baldassarre, G., Bassi, P., Trapasso, F., Alder, H., Pagano, F., Gomella, L. G., Croce, C. M., and Baffa, R. FEZ1/LZTS1 is down-regulated in high-grade bladder cancer, and its restoration suppresses tumorigenicity in transitional cell carcinoma cells, Am J Pathol. 2002, Apr, 160 (4): 1345-52.
8. Wilkinson, S., Gomella, L. G., Smith, J. A., Brawer, M. K., Dawson, N.A., Wajsman, Z., Dai, L., and Chodak, G. W. Attitudes and use of complementary medicine in men with prostate cancer, J Urol. 2002, Dec; 168 (6): 2505-9.
9. Moreno, JG, O'Hara, SM, Gross, S, Doyle G, Fritsche H, Gomella LG, Terstappen LW. Changes in circulating cells in patients with metastatic prostatic cancer correlate with disease status. Urology, 2001 Sep;58(3):386-92
10. Gomella, LG, Mastrangelo MJ, McCue, PA, Maguire HC Jr., Mulholland, SG, Phase 1 study of intravesical vaccinia virus as a vector for gene therapy of bladder cancer. J Urol. 2001, Oct; 166(4):1291-5
11. Ismail, M, Gomella, LG, Ultrasound for prostate imaging and biopsy. Curr Opin Urol, 2001 Sep;11(5):471-7. Rev
12. Chen, CT, Waterman, FM, Valicenti, RK, Gomella, LG, Strup SE and Dicker, AP Dosimetric analysis of urinary morbidity following prostate brachytherapy (I-125 vs. Pd-103) combined with external beam radiation therapy. Int J Cancer, 2001; 96 Suppl: 83-8
13. Gomella LG Minimally Invasive Urologic Oncology, A New Sub Specialty? Editorial, Tech Urol 2001, 7(1):1
14. Valicenti RK, Chen CT, DeRose T, Lu JD, Mulholland SG, Hirsch IH, Gomella LG Sildenafil Citrate Effectively Reverses Sexual Dysfunction Induced By 3D Conformal Radiation Therapy, Urology 2001 Apr;

57(4): 769-73
15. Halpern, E. J, Rosenberg, M, and Gomella, LG Prostate Cancer: Contrast-enhanced US for Detection Radiology 2001, Apr ; 219 (1):219-225
16. Dicker AP, Figura AT, Waterman FM, Valicenti RK, Strup SE, Gomella LG. Is There a Role for Antibiotic Prophylaxis in Transperineal Interstitial Permanent Prostate Brachytherapy? Tech Urol, 2000; 6(2):104-8
17. Valicenti RK, Gomella LG. Durable Efficacy of Adjuvant Radiation Therapy for Prostate Cancer: Will the Benefit Last? Seminars in Urologic Oncology, 2000, 18(2):115-120.
18. El-Gabry, EA, Strup, SE and Gomella, LG Deciding on Radical Prostatectomy, the Physicians Perspective. Semin Urol Oncol, 2000 Aug;18(3):205-13
1. Gomella LG, Albertsen P, Benson M, Forman J, Soloway M. " The Use of Video-Based Patient Education For Shared Decision-Making In the Treatment of Prostate Cancer Semin Urol Oncol, 2000 Aug;18(3):182-7
2. Valicenti RK, Gomella LG, Strup SE, Nathan FE, Dick A, Cardi N, McGinnis DE, Baltish, MA Simiriglio M, Vizzard A, Mulholland, SG. The Multidisciplinary Clinic Approach to Prostate Cancer Semin Urol Oncol, 2000 Aug;18(3):188-91
3. London J, Gomella LG. Internet Prostate Cancer Resources Semin Urol Oncol. 2000 Aug;18(3):245-53
4. Gomella, LG The Wild, Wild Web: Challenges of Counseling prostate cancer patients in the Information Age Semin Urol Oncol, 2000 Aug;18(3):167-71
5. Rivas DA, Bagley D, Gomella LG, Hirsch IH, Hubert C, Lombardo S, McGinnis DE, Mulholland SG, Shenot PJ, Strup SE, Vasavada SP, TJUH TUMT Study Group. Transurethral Microwave Thermotherapy (TUMT) of the Prostate Without IV Sedation: Results of a Single U.S. Center using Both Low- and High-Energy Protocol. Tech Urol. 2000 Dec;6 (4):282-7.
6. El-Gabry, E.A., Strup, S.E., Gomella, L.G., "Undetectable PSA Response with Bicalutamide (Casodex) Withdrawal Phenomenon Tech Urol, 2000 Sep;6(3):221-2
7. Mastrangelo MJ, Eisenlohr LC, Gomella LG, Lattime EC. Poxvirus vectors: Orphaned and under appreciated. J Clin Invest, 2000;105(8):1031-1034.
8. Chen CT, Valicenti RK, DeRose T, Lu JD, Strup SE, Mulholland SG, Hirsch IH, Gomella LG, Serial evaluation of sexual function before and after 3D conformal radiation therapy for prostate cancer. Int J Radiat Oncol Biol Phys, 2000, Jul, 1;50 (3) 591-5
9. Kunkel EJ, Bakker JR, Myers RE, Oyesanmi O, Gomella LG. Biopsychosocial aspects of prostate cancer. Psychosomatics, 2000, Mar-Apr; 41(2):85-95.
10. Halpern EJ, Verkh L, Forsberg F, Gomella LG, Mattrey RF, Goldberg BB. Initial Experience with Contrast-Enhanced Sonograph of the Prostate. Am J Roentgenol 2000, June; 174(6):1575-80.
11. Baffa R, Gomella, LG, Vecchione A, Bassi P, Mimori K, Sedor J, Calviello CM, Gardiman M, Minimo C, Strup SE, McCue PA, Kovatich AJ, Pagano F, Huebner K, Croce CM, Loss of FHIT expression in transitional cell carcinoma of the urinary bladder. Am J Pathol, 2000, Feb; 156(2):419-24
12. Nasuti JF, Gomella LG, Ismail M, Bibbo M. Utility of the BTA stat test kit for bladder cancer screening. Diagn Cytopathol. 1999 Jul;21(1):27-9
13. Valicenti RK, Gomella LG, Ismail M, Mulholland SG, Petersen RO, Corn BW, Effect of higher radiation dose on biochemical control after radical prostatectomy for PT3N0 prostate cancer, Int J Radiat Oncol Biol Phys, 1998 Oct 1; 42(3):501-6. Review
14. Moreno JG, Gomella LG Circulating Prostate Cancer Cells detected by reverse transcription-polymerase chain reaction (RT-PCR): What do they mean? Cancer Control 1998 Nov; 5(6):507-12

RESEARCH SUPPORT.

Urology Chair
American College of Radiology — Period: 07/01/99-present
RTOG Core Grant

Principal Investigator — Period: 09/1989 - present
Longitudinal Study to determine the utility of PSA as a test for the early detection of Prostate Cancer
The purpose of the study is to determine if prostate specific antigen (PSA) blood test has value as a test for the early detection of prostate cancer. Changes in PSA values among study participants over time will be assessed for effectiveness in the early detection of prostate cancer.

Principal Investigator
NCI through SWOG Period: 02/01/01-1/31/06
Selenium and Vitamin E Cancer Prevention Trial (SELECT A)
This is a placebo-controlled trial for the prevention of prostate cancer using selenium or the combination of selenium and vitamin E.

Principal Investigator
Novartis Period: 03/15/03-03/15/05
The Effect of Zometa Compared to Placebo on Bone Mineral Density in Patients Undergoing Androgen Deprivation Therapy
To compare the effect of intravenous Zometa (zoledronic acid) 4 mg and placebo administered every 3 months for one year, on bone loss associated with initial androgen deprivation (ADT) (LHRH agonist with or without another antiandrogen agent or orchiectomy) in men with non metastatic prostate carcinoma.

Principal Investigator
Antigenics Period: 07/22/03 - present
A Multi-Center, Randomized Phase III Study of Adjuvant Oncophage® versus Observation in Patients with High Risk of Recurrence After Surgical Treatment for Renal Cell Carcinoma.
HSPPC-96, Oncophage®, is an active, specific immunotherapy that uses renal tumor cells isolated from the patient's own tumor following surgical resection. Post-operative vaccination of the patient with Oncophage® will provide a highly unique, individualized treatment option that may prevent or delay subsequent tumor progression. The purpose of this study is to determine if patients who are treated with Oncophage® for surgically resected, locally advanced renal cell carcinoma have a statistically longer survival than those who do not receive the vaccination.

Principal Investigator
Dendreon Period: 09/04/03 - present
A Randomized, Double Blind, Placebo Controlled Phase 3 Trial of Immunotherapy with Autologous Antigen Presenting Cells Loaded with PA2024 (Provenge®, APC8015) in Asymptomatic Subjects with Gleason Sum = 7, Metastatic, Androgen Independent Prostatic Adenocarcinomas
This trial evaluates a new approach to prostate cancer treatment using an autologous cell product consisting of antigen presenting cells (APCs) loaded with prostate antigen PA2024, a recombinant fusion protein composed of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF). Previous research has shown that benefit was primarily confined to subjects with Gleason Sum = 7 malignancies. In short, this study uses a subject's own cells that are responsible for stimulating certain immune responses. These cells have attached to the proteins that may direct a person's immune reaction towards prostate cancer cells.

COMPLETED
Principal Investigator
PhotoCure Period: 3/02-10/03
An Open Comparative within Patient Controlled Phase III Multicenter Study of Hexvix® Fluorescence Cystoscopy and Standard Cystoscopy in the Detection of Carcinoma in Situ in Patients with Bladder Cancer
The aim of the study is to see if this new drug, Hexvix® used with blue light cystoscopy, helps doctors to improve the detection of bladder cancers, when compared to white light (standard) cystoscopy in patients with bladder cancer. The study will also aim to show that the new drug is safe. This study will also compare Hexvix® cystoscopy with standard cystoscopy in the detection of carcinoma in situ (CIS) in patients with bladder cancer.

Co-Investigator (PI: R. Myers, MD)
NIH Period: 07/01-4/03
Increased Access to Clinical and Educational Studies

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Raffaele Baffa, M.D.	Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Padova, Italy	M.D.	1987	Medicine

Positions and Employment

10/87-12/91 Residency in Pathology, Department of Pathology, University of Trieste, Italy
7/88-12/88 Visiting Scientist, Department of Cytopathology, Dr. Zajdela Laboratory, Curie Institute, Paris
1/91-6/91 Visiting Scientist, Department of Pathology, Dr. Ming Laboratory, Temple University, Philadelphia, PA
6/90-6/93 Assistant Professor, Pathology Department, Cittadella Hospital, University of Padova, Italy.
7/93-6/97 Research Fellow, Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA
7/97-6/02 Assistant Professor of Urology and Microbiology and Immunology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
7/02-pre. Associate Professor of Urology and Microbiology and Immunology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
6/98-pre. Co-Director Genito-Urinary Cancer Program, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
7/02-pre. Director of Urology Research, Department of Urology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Honors

2001 Kimmel Scholar, Sidney Kimmel Foundation for Cancer Research

Publications (1995 to present)

1. D'Andrea E., Baffa R., Menin C., Montagna M., Rugge M., Chieco-Bianchi L. TP53 gene mutations in gastric carcinoma detected by polymerase chain reaction/single-strand conformation polymorphism analysis of archival material. J.Cancer Res. Clin. Oncol. 121: 79-83, 1995.
2. Baffa R., Negrini M., Schichman S., Huebner K., Croce C.M. Involvement of *ALL-1* in a solid tumor. Proc. Natl. Acad. Sci. USA 92:4922-4926, 1995.
3. Negrini M., Cuneo A., Nakamura T., Alder H., Sabbioni S, Baffa R., Castoldi G., and Croce C. M. A novel t(9;11)(p22;q23) chromosome translocation with *ALL-1* gene rearrangement associated with the progression of a myeloproliferative disorder to acute myeloid leukemia. Cancer Genet. Cytogenet. 83:65-70, 1996.
4. Baffa R., Negrini M., Mandes B., Rugge M., Ranzani G.N., Hiroshashi S., Croce C.M. Loss of hetrozygosity for chromosome 11 in adenocarcinoma of the stomach. Cancer Res. 56:268-272, 1996.
5. Ohta M., Inoue H., Cotticelli M.G., Kastury K., Baffa R., Palazzo J., Siprashvilli Z., Mori M., McCue P., Druck T., Croce C.M., Huebner K. The human *FHIT* gene, spanning the chromosome 3p14.2 fragile site and renal carcinoma associated translocation breakpoint, is abnormal in digestive tract cancer. Cell 84:587-597, 1996.
6. Kastury K., Baffa R., Druck T., Ohta M., Coticelli M.G., Inoue H., Negrini M., Rugge M., Huang D., Croce C.M., Palazzo J., Huebner K. Potential gastrointestinal tumor suppressor locus at 3p14.2 *FRA3B* site identified by homozygous deletions in tumor cell lines. Cancer Res. 56:978-983, 1996.

7. Sozzi G., Veronose M.L., Negrini M., Baffa R., Coticelli MG., Inoue H., Tornielli S., Pilotti S., De Gregorio L., Pastorino U., Pierotti M.A., Ohta M., Huebner K., Croce C.M. The *FHIT* gene at 3p14.2 is abnormal in lung cancer. Cell 85:17-26, 1996.
8. Baffa R., Moreno J.G., Monne M., Veronese M.L., Gomella L.G. A compariative analysis of prostate specific antigen gene sequence in benign and malignant prostate tissue. Urology 47(6):795-800,1996.
9. Rugge M., Cassaro M., Leandro G., Baffa R., Avellini C., Bufo P., Stracca V., Battaglia G., Fabiano A., Guerini A., Di Mario F. Helicobacter pylori in promotion of gastric carcinogenesis. Dig. Dis. Sci.. 41(5):950-955, 1996.
10. Sozzi G., Alder H., Tornielli S., Corletto V., Baffa R., Veronese M.L., Negrini M., Pilotti S., Pierotti M., Huebner H., Croce C.M. *FHIT* aberrant transcripts in Merkel cell carcinoma. Cancer Res. 56:2472-2474, 1996.
11. Druck T., Hadaczek P., Fu T-B., Ohta Z., Siprashvili R., Baffa R., Negrini M., Veronese M.L., Rosen D., Rothstein J., McCue P., Cotticelli M.G., Inoue H., Croce C.M., Huebner K. Structure and expression of the human *FHIT* gene in normal and tumor cells. Cancer Res. 57:504-512, 1997.
12. Negrini M., Monaco C., Vorechovky I., Ohta M., Druck T., Baffa R., Huebner K., Croce C.M. The *FHIT* gene at 3p14.2 is abnormal in breast carcinomas. Cancer Res. 56:3173-3179, 1996.
13. Schmutte C., Baffa R., Veronese L.M., Murakumo Y., Fishel, R. Human Thymine-DNA glycosylase maps at chromosome 12q24: a region of high LOH in gastric Cancer. Cancer Res. 57:3010-3015, 1997.
14. Busatto G., Shiao Y.H., Parenti A.R., Baffa R., Ruol A., Plebani M., Rugge M. *p16/CDKN2* alterations and *pRb* expression in oesophageal squamous carcinoma. Mol. Pathol. 51(2):80-84, 1998.
15. Baffa R., Veronese M.L., Santoro R., Mandes B., Palazzo J.P., Rugge M., Santoro E., Croce C.M., Huebner K. Loss of *FHIT* expression in gastric carcinomas. Cancer Research. 58:4708-4714, 1998.
16. Ishii H., Baffa R., Numata S., Murakumo Y., Inoue H., Mori M., Alder H., Croce C.M. *FEZ1* gene at chromosome 8p22 encoding a leucine-zipper protein: its altered expression in multiple human tumors. Proc. Natl. Acad. Sci. USA 96:3928-3933, 1999.
17. Capuzzi D., Santoro E., Hauck W.W., Kovatich A.J., Rosato F.E., Baffa R., Huebner K., McCue P.A. (1999). *Fhit* expression in gastric adenocarcinoma:correlation with disease stage and survival. Cancer 88:24-34, 2000.
18. Baffa R., Gomella L.G., Vecchione A., Bassi P., Mimori K., Sedor J., Calviello C.M., Gardiman M., Minimo C., Strup S.E., McCue P.A., Kovatich A.J., Pagano F., Huebner K., and Croce C.M. Loss of *Fhit* expression in Transitional Cell carcinoma (TCC) of the urinary bladder. Am. J. Pathol. 156:419-424, 2000.
19. Baffa R., Santoro R., Bullrich F., Mandes B.M., Ishii H., and Croce C.M.. Loss of heterozygosity for chromosome 8p in adenocarcinoma of the stomach. Clin Cancer Res. 6:1372-1377, 2000.
20. Baffa R., Reiss K., El-Gabry E. A., Sedor J., Moy M.L., Shupp-Byrne D., Strup S.E., Hauch W.W., Baserga R., and Gomella L. G. Serum insulin-like growth factor I (IGF-I) is decreased in patients with prostatic cancer. Tech. Urol. 6:236-239, 2000.
21. H. Ishii, K. Dumon, A. Vecchione, F. Trapasso, K. Mimori, H. Alder, M. Mori, G. Sozzi, R. Baffa, K. Huebner, and C. M. Croce (2001). *Effect of adenoviral transduction of FHIT into esophageal cancer cells.* Cancer Res. 61:1578-1584
22. K. Dumon, H. Ischii, N. Zanesi, V. Fidanza, A. Vecchione, V.T. Nguyen, R. Baffa, F. Trapasso, M. During, L. Y. Fong, K. Huebner, and C. M. Croce (2001). *FHIT gene therapy prevents tumor development in thit-deficient mice.* Proc. Nati. Acad. Sci. USA 98:3346-335 1
23. A. Vecchione, H. Ishii, Y-H. Shiao, F. Trapasso, M. Rugge, H. Alder, C. M. Croce, and R. Raffa (2001). *Fez1/Lztsl alterations in Gastric Carcinoma.* . Clin Cancer Res 7:1546-1552
24. H. Ishii, A. Vecchione, Y. Murakumo, G. Baldassarre, S. Numata, F. Trapasso, H. Alder, R. Baffa, and C. M. Croce (2001). *FEZ1/LZTS1 gene suppresses cancer cell growth and regulates mitosis.* Proc. Natl. Acad. Sci. USA 98(18):10374-9
25. H. Ishii, K. R. Dumon, A. Vecchione, L.Y.Y. Fong, R. Baffa, K. Huebner, and C. M. Croce (2001). *Cancer therapy by introduction of the FHIT gene: pre-clinical studies.* JAMA. 286:2441-2449
26. A. Vecchione, H. Ishii, G. Baldassarre, P. Bassi, F. Trapasso, H. Alder, F. Pagano, L. G. Gomella, C. M. Croce and R. Baffa (2002). *FEZ1/LZTS1* is down regulated in high-grade bladder cancer, and its restoration suppresses tumorigenicity in transitional cell carcinoma (TCC) cells. Am. J. Pathol. 160: 1345-1352
27. M. Prisco, F. Santini, R. Baffa, M. Liu, R. Drakas, A. Wu, and R. Baserga (2002). Nuclear translocation of IRS-1 by the SV40 T antigen and the activated IGF-I receptor. J. Biol. Chem. 277: 32078-32085
28. G. Pistritto, M. Jost, S. M. Srinivasula, R. Baffa, C. Kari, U. Rodeck, and E. S. Alnemri (2002). Expression and transcriptional regulation of caspase-14 in simple and complex epithelia. Cell Death Differentiation

9:995-1006
29. X. Tu, R. Baffa, S. Luke, M. Prisco, and R. Baserga (2003). Intracellular redistribution of nuclear and nucleolar proteins during differentiation of 32D murine hemopoietic cells. Exp Cell Res. 288(1):119-30
30. H. Ishii, N. Zanesi, A. Vecchione, F. Trapasso, S. Yendamuri, M. Sarti, R. Baffa, M.J. During, K. Huebner, L.Y. Fong, and C.M. Croce (2003). Regression of upper gastric cancer in mice by *FHIT* gene delivery. FASEB J. 17(12):1768-70
31. E.M. Gonzalez, M. Mongiat, S.J. Slater, R. Baffa, and R.V. Iozzo (2003). A novel interaction between perlecan protein core and progranulin: Potential effects on tumor growth. J Biol Chem. 278(40):38113-38116.
32. H. Ishii, A. Vecchione, L.Y.Y. Fong, N. Zanesi, F. Trapasso, Y. Furukawa, R. Baffa, K. Huebner, and Carlo M. Croce. Cancer Prevention and Therapy in a Preclinical Mouse Model: Impact of *FHIT* Viruses. In Press *Current Gene Therapy*, 2004, *Vol. 4, No. 1.*
33. R. I. Aqeilan, T. Kuroki, Y. Pekarsky, O. Albagha, F. Trapasso, R. Baffa, K. Huebner, P. Edmonds,and C. M. Croce (2004). Loss of *WWOX* Expression in Gastric Carcinoma. Clin. Cancer Res. 10: 3053-3058

Completed Research Support:

"Analysis of TS12Q, A Novel Putative Tumor Suppressor Gene at Chromosome 12q24"
P.I. Raffaele Baffa
Agency: Sidney Kimmel Foundation (7/1/2001-6/30/2003)
The main goal was to determine if the TS12Q gene, a novel gene that we have previously identified at chromosome 12q24.1, a region frequently deleted in several cancers, is a legitimate tumor suppressor gene.

Ongoing Research Support:

Project II Aerodigestive and Bladder Cancer- Commonwealth Universal Research Enhancement (C.U.R.E.) program, Raffale Baffa Co.P.I. (2/01/02-12/31/05)
The main purpose of this project is to accomplish a molecular characterization of carcinoma of the urinary bladder in order to identify appropriate molecular markers for an early diagnosis and a better follow-up of this disease, and to characterize novel targets for multi-modality therapies.

COXIB Medical School Grants Program, Merck
P.I. Raffaele Baffa (12/10/03-12/09/05)
" Rofecoxib and inhibition on N-Butyl-N-(4-hydroxybutyl)-nitrosamine induced urinary bladder cancer in FHIT negative mice"
The major goal of this project is to investigate the role of rofecoxib in the prevention and treatment of bladder cancer in fhit knock-out mice

CURRICULUM VITAE
CHRISTINE D. HUBERT, B.A.
09/16/04

PRESENT TITLE:	Clinical Study Coordinator Thomas Jefferson University Department of Urology Philadelphia, PA
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CITIZENSHIP:	USA
UNDERGRADUATE EDUCATION:	Rutgers University 1990-94 B.A.
GRADUATE EDUCATION:	Thomas Jefferson University, College of Graduate Studies January 2000 – present MS in Pharmacology/Research Scientist
PREVIOUS EMPLOYMENT:	Research Associate Cooper Hospital Department of Gastroenterology Camden, NJ 1994-99
ASSOCIATIONS:	Association of Clinical Research Professionals, 1999 - present Jefferson Clinical Research Association, Member since 1999

PUBLICATIONS: Original Articles:

Rivas DA. Bagley D. Gomella LG. Hirsch IH. **Hubert** C. Lombardo S. McGinnis DE. Mulholland SG. Shenot PJ. Strup SE. Vasavada SP. Transurethral microwave thermotherapy of the prostate without intravenous sedation: results of a single United States center using both low- and high-energy protocols. TJUH TUMT Study Group. Techniques in Urology. 6(4):282-7, 2000.

Spiegel, T.A., , Fried, H., **Hubert, C.D.** Peikin, S.R.,Siegel, J.A.,Zeiger, L.S. Effects of posture on gastric emptying and satiety ratings after a nutritive liquid and solid meal. Am J of Physiol 2000; 279(2):R684-94.

Spiegel, T.A., **Hubert, C.D.**, Fried, H., Peikin, S.R., Siegel, J.A., Zeiger, L.S. Contribution of gastric and Postgastric feedback to satiation and satiety in Women. Physiol & Behav 1997; 62(5):1125-1136.

Abstracts:

Spiegel, T.A., **Hubert, C.D.**, Peikin, S.R. Haloperidol Increases lunch intake in lean but not obese men. Proceedings & Abstracts of the Annual Meeting of The Eastern Psychological Association 1997; 68:26.

Spiegel, T.A., Siegel, J.A., **Hubert, C.D.**, Peikin, S.R.. Effect of posture on gastric emptying in women. Appetite 1997; 29(3):392.

Spiegel, T.A., Peikin, S.R., **Hubert, C.D**. Effects of Metoclopramide on food intake in normal-weight Men. Appetite 1998.

GRANTS

Prospective, Randomized, Double-Blind, Comparison of Ciprofloxacin Extended-Release 1000 Mg Tablets Given as Two Different Prophylactic Dosing Regimens (Regimen I- Single-Dose Ciprofloxacin MR 1000 Mg or Regimen II- Multiple-Dose Ciprofloxacin MR 1000 Mg Once Daily for 3 Days) for the Prevention of Post-Operative Infectious Complications in Patients Undergoing Transrectal Needle Biopsy of the Prostate.
Bayer Pharmaceuticals. Study Coordinator 2004 – present.

A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer.
GlaxoSmithKline. Study Coordinator 2004 – present.

A Randomized, Double Blind, Placebo Controlled Phase 3 Trial of Immunotherapy with Autologous Antigen Presenting Cells Loaded with PA2024 (Provenge®, APC8015) in Asymptomatic Subjects with Gleason Sum ≤7, Metastatic, Androgen Independent Adinacarcinomas.
Dendreon. Study Coordinator 2003 – present.

Study of the Safety and Effectiveness of the Mentor Two-Piece Inflatable Penile Prosthesis.
Mentor, Corp. Study Coordinator 2003 – present.

A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of RTX Topical Solution in Patients with Interstitial Cystitis.
ICOS, Inc. Study Coordinator 2003-present.

A Multi-Center, Randomized Phase III Study of Adjuvant Oncophage® versus Observation in Patients with High Risk Of Recurrence after Surgical Treatment for Renal Cell Carcinoma.
Antigenics, Inc. Study Coordinator 2002-present.

A Multi-Center, Open-Label, Flexible Dose Escalation Study to Evaluate the Correlation Between Event Log Parameters, Self-Esteem/Overall Relationships (SEAR), and Efficacy of Viagra (Sildenafil Citrate) in Men with Erectile Dysfunction.
Pfizer, Inc. Study Coordinator 2002-present.

A Double-Blind, Placebo-Controlled, Randomized US Study to Evaluate the Effect of Tolterodine Prolonged Release on Nocturia in Patients with Symptoms of Overactive Bladder (OAB).
Pharmacia. Study Coordinator 2002-present.

An Open Comparative within Patient Controlled Phase III Multicenter Hexvix Fluorescence Cystoscopy and Standard Cystoscopy in the Detection of Carcinoma in Situ in Patients with Bladder Cancer PC B 302/01
PhotoCure, Inc Study Coordinator 2002-present

The Safety, Local Tolerability, Pharmacokinetics, and Risk/Benefit of Oxybutynin Transvaginal Rings (TVR) 6 mg/day in Women with a History of Overactive Bladder
FEI Technologies, Inc. Study Coordinator 2001-2002.

A Post-Market Clinical Study Evaluating the Uroflow, PVR, and Symptoms Alleviation of Water Induced Thermotherapy with the Thermoflex System.
Argomed. Study Coordinator 2000-2001.

Urodynamic Response to Treatment with Ditropan XL in Patients with Detrusor Hyperreflexia.

Alza Corporation. Study Coordinator 2000-present.

A Phase III, Multicenter, Open Label Continuation Study of the Longterm Safety, Toleration, compliance and Efficacy of Controlled Release Darifenacin in Subjects with Overactive Bladder. Pfizer, Inc.
Study Coordinator 2000-2002

A Patient Acceptability Study of Once-Daily Formulation of Tolterodine. A Phase IIIB Open-Label Single Arm Trial in Adult Patients with Overactive Bladder and Symptoms of Urinary Frequency, Urgency and/or Urge Incontinence.
Pharmacia & Upjohn. Study Coordinator 2001.

A Phase III, Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Controlled-Release Darifenacin Versus Tolterodine in the Treatment of Subjects with Overactive Bladder.
Pfizer, Inc. Study Coordinator 2000-2001.

A Randomized, Parallel-Group, Double-Blind, Placebo-Controlled Study Comparing the Safety, Tolerance, and Efficacy of RTX (resiniferatoxin) Topical Solution in Patients with Detrusor Hyperreflexia.
Afferon Corporation. Study Coordinator 2000 – 2001.

Post Approval Sacral Nerve Stimulation Study for the Treatment of Urinary Voiding Dysfunction.
Medtronic, Inc. Study Coordinator 1999 – present.

A Prospective Evaluation of the Urethral Drainage Stent (UDS) for patients with Urinary Retention Secondary to Prostate Obstruction.
Boston Scientific. Study Coordinator 1999 – 2001.

An Open Label Study to Evaluate Patient Acceptance and Safety of OROS Oxybutynin Chloride in Urge Urinary Incontinence.
Alza Corporation. Study Coordinator 1999 - 2000.

Dose Escalating Study with Tolterodine in Patients with Overactive Bladder. A single blind study in patients with symptoms or overactive bladder including urinary urgency and frequency with or without urge incontinence.
Pharmacia & Upjohn. Study Coordinator 1999.

Intron A & Ribavirin for Treatment of Patients with Chronic Hepatitis C not Previously treated with Interferon.
Schering Corporation. Study Coordinator 1998 – 1999.

Combination Therapy with Interferon alpha 2b and Ribavirin for Chronic infection with Hepatitis C Virus.
Schering Corporation. Study Coordinator 1997 - 1999.